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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/665,671	09/19/2003	Mark R. Andersen	4987	8573

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EXAMINER	
WHISENANT, ETHAN C	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 02/13/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/665,671	ANDERSEN ET AL.	
	Examiner	Art Unit	
	Ethan Whisenant, Ph.D.	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 November 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-44* is/are pending in the application.

4a) Of the above claim(s) *29-34* is/are withdrawn from consideration.

5)☒ Claim(s) *1-21, 27-28, 35-37* is/are allowed.

6)☒ Claim(s) *22-26 and 41-44* is/are rejected.

7)☒ Claim(s) *38-40* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 September 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

NON-FINAL ACTION

1. Applicant's election of Group I (**Claims 1-28 and 35-44**) without traverse in the paper(s) filed 25 NOV 05 is acknowledged. Claim(s) 29-34 is/are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. The restriction requirement has been reconsidered, is deemed proper and is therefore, herein made **FINAL**.

SEQUENCE Rules

2. This application fails to comply with the sequence rules. See the attached notice to comply with the sequence rules.

35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> **(a)** A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligations under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

CLAIM REJECTIONS UNDER 35 USC § 103

5. **Claim(s) 22-24** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Schouten et al. [US Patent No. 6,955,901 (2005)] in view of Wittwer [US 6,387,621 (2002)].

Schouten et al. teach a method for detecting at least one target nucleic acid sequence in a sample which comprises all of the limitations recited in Claim 22, see especially Column 17, beginning at about line 19, except this reference does not teach detecting a second detectable signal value at least one of during and after the amplification reaction, wherein a threshold difference between the first detectable signal value and the second detectable signal value indicates the presence of the target nucleic acid sequence, and wherein no threshold difference between the first detectable signal value and the second detectable signal value indicates the absence of the target nucleic acid sequence. However Wittwer does teach a method (i.e. real-time quantitative PCR) wherein a second detectable signal value is detected at least one of during and after the amplification reaction, wherein a threshold difference between the first detectable signal value and the second detectable signal value indicates the presence of the target nucleic acid sequence, and wherein no threshold difference between the first detectable signal value and the second detectable signal value indicates the absence of the target nucleic acid sequence. Therefore, absent an unexpected result, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method of Schouten et al. wherein the ligation product is detected by the method disclosed by Wittwer. The motivation to combine comes from Schouten et al. in Column 17 wherein these authors teach detecting the ligation product of their method "using real-time quantitative PCR with the use of molecular beacons as marketed by Stratagene Corp." As regards the limitation(s) recited above, see, at least, for example, the abstract of Wittwer.

Claim 23 is drawn to an embodiment of Claim 22 wherein the reaction composition further comprises a ligation reagent, wherein the ligation reagent activity is substantially destroyed prior to the at least one amplification reaction. **Claim 24** is drawn to an embodiment of Claim 23 wherein the ligation reagent activity is substantially destroyed by subjecting the reaction composition to a temperature for a time period that substantially destroys the ligation reagent activity.

Schouten et al. teach these limitations (see Column beginning at about line 5) wherein these authors teach "In a preferred embodiment of the current invention said ligation is performed with a thermostable nucleic acid ligase active at temperatures of 50°C. or higher, but capable of being rapidly inactivated above approximately 95°C. Once probes are connected it is preferred that essentially no connecting activity is present during amplification since this is not required and can only introduce ambiguity in the method."

6. **Claim(s) 25-26** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Schouten et al. [US Patent No. 6,955,901 (2005)] in view of Wittwer [US 6,387,621 (2002)] as applied to Claims 22-24 above and further in view of Chen et al. [Vox Sanguinis 72 :192-196 (1997)].

Claim 25 is drawn to an embodiment of Claim 22 wherein the polymerase is substantially inactive during the at least one cycle of ligation and the polymerase is activated for the at least one amplification reaction. **Claim 26** is drawn to an embodiment of Claim 25 wherein the polymerase is activated by subjecting the reaction composition to a temperature for a time period that activates the polymerase.

The method reasonably suggested by the combination of Schouten et al. in view of Wittwer comprises all of the limitations recited in Claim 25 except these authors do not teach using a polymerase that is activated for the at least one amplification reaction. However, Chen et al. do teach a polymerase that is activated prior to its use in a PCR. Please note that substitution of one well known method/reagent with known properties for a second well known method/reagent with well known properties would have been *prima facie* obvious to the ordinary artisan at the time of the invention in the absence of an unexpected result. As regards the motivation to make the substitution recited above, the motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Support for making this obviousness rejection comes from the M.P.E.P. at 2144.07 and 2144.09.

7. **Claim(s) 41-44** is/are rejected under 35 U.S.C. 103(a) as being unpatentable over Barany et al. [US Patent No. 6,027,889 (2000)] in view of Kutayvin et al.[Nucleic Acids Research 28(2):655-661(2000)].

Barany et al. teach a method for detecting at least one target nucleic acid sequence in a sample which comprises all of the limitations recited in Claim 41-44, see at least for example, the abstract; except this reference does not teach a minor groove binder attached to the one or both of the probes and/or primers. However, Kutayvin et al. do teach probes/primers with attached minor groove binder as well as the fact that such probes/primers show increased sequence specificity at PCR extension temperatures. Therefore, absent an unexpected result, it would have been *prima facie* obvious to one of ordinary skill in the art at the time of the invention to modify the method of Barany et al. wherein minor groove binders are attached to the probes/primers. The motivation to combine comes from Kutayvin et al. who teach "MGB probes were more specific than standard DNA probes , especially for single base mismatches at elevated hybridization temperatures."

CLAIM OBJECTIONS

8. **Claim(s) 38-40** is/are objected under 37 CFR 1.75 as being a substantial duplicate of Claims 25-37. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

REASON FOR ALLOWANCE

9. **Claims 1-21,27-28, 35-40** are allowable over the prior art of record because the prior art considered does not teach or reasonably suggest the method for detecting at least one target nucleic acid sequence in a sample as recited in Claims 1, 27, 28 or the kit recited in Claim 35 and 38 In particular, the closest prior art Schouten et al. [US Patent No. 6,955,901 (2005)] and/or Barany et al. [US Patent No. 6,027,889 (2000)] do not teach or reasonably suggest, either alone or in combination with the other prior art considered, the method for detecting at least one target nucleic acid sequence in a sample as recited in Claims 1, 21 and 27 and 28 or the kit recited in Claims 35 and 38 wherein each of the ligation probes comprise an addressable portion located in between a target specific portion and a primer specific portion.

CONCLUSION

8. **Claim(s) 1-21, 27-28, 35-37** is/are allowable while Claim(s) 22-26, and 38-44 is/are rejected and/or objected to for the reason(s) set forth above.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ethan Whisenant, Ph.D. whose telephone number is (571) 272-0754. The examiner can normally be reached Monday-Friday from 8:30AM -5:30PM EST or any time via voice mail. If repeated attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached at (571) 272-0745.

The Central Fax number for the USPTO is (571) 273-8300. Before faxing any papers, please inform the examiner to avoid lost papers. Please note that the faxing of papers must conform with the Notice to Comply published in the Official Gazette, 1096 OG 30 (November 15, 1989).

ETHAN WHISENANT
PRIMARY EXAMINER
Art Unit 1634

Application No.: 10/665 ,671

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

■ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to these regulations, published at 1114 OG 29, May 15, 1990 and at 55 FR 18230, May 1, 1990.

□ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

□ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

■ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked-up "Raw Sequence Listing."

□ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

□ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

□ 7. Other:_____

Applicant Must Provide:

■ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

■ An initial or substitute paper copy of the "Sequence Listing", as well as, an amendment directing its entry into the specification.

■ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).